to 20 cigarettes a day) in September, 1951. In another instance, the doctor had described himself as smoking 3½ oz. of pipe tobacco a week, but a friend, who signed the death certificate and had known him for 25 years, stated he had previously been one of the heaviest smokers of both cigarettes and pipe he had ever known. Such factors not only could not produce an exaggeration of the true relationship but must lead to an understatement of it by inflating the mortality among light smokers and reducing the mortality among heavy smokers.

The investigation has not, as yet, continued long enough to show whether there is a relationship between smoking and the mortality from any other disease, but from the preliminary figures it would seem unlikely that there is any as close as that observed with lung cancer. The numbers of deaths, however, from some potentially interesting diseases are as yet small (for example, from cancer of the buccal cavity and larynx and from duodenal ulcer). There have, on the other hand, been a large number of deaths attributable to coronary thrombosis. It seems clear that smoking cannot be a major factor in their production, but the steady increase in mortality with the amount of tobacco smoking recorded suggests that there is a subgroup of these cases in which tobacco has a significant adjuvant effect.

Summary

At the end of 1951 some 40,000 men and women on the British *Medical Register* replied to a simple questionnaire relating to their smoking habits. On that basis they were divided into non-smokers and three groups of smokers (including ex-smokers) according to the amount they smoked at that time (or when they gave up).

The certified causes of death of those men and women who have since died have been supplied by the Registrars-General of the U.K. over the ensuing 29 months. This preliminary report is confined to the deaths among the 24,389 men over the age of 35.

Though the numbers of deaths at present available are small the resulting rates reveal a significant and steadily rising mortality from deaths due to cancer of the lung as the amount of tobacco smoked increases. There is also a rise in the mortality from deaths attributed to coronary thrombosis as the amount smoked increases, but the gradient is much less steep than that revealed by cancer of the lung. The other groups of deaths so far analysed reveal no gradient (other forms of cancer, other forms of cardiovascular disease, respiratory diseases, all other causes).

The figures for cancer of the lung are in conformity with those found previously in an extensive inquiry into the smoking histories of patients with cancer of the lung and with other diseases.

The death rates of doctors here reported are, almost certainly, artificially low. There is evidence that this is due to a reluctance, or inability, of persons suffering from a fatal illness to reply to the questionnaire. In spite of this defect and the present small numbers of deaths, we thought it necessary, in view of the nature of the results, to lay these preliminary observations before the survivors of the 40,000 men and women who made them possible.

We are most grateful to the British Medical Association for having dispatched the questionnaires and letters to the doctors on our behalf; to the individual doctors for having completed the questionnaires; and to those practitioners and consultants to whom we wrote for details of the evidence on which the diagnosis of lung cancer was made. We are deeply indebted to the Registrars-General of the United Kingdom for information about the deaths of doctors. We also offer our thanks to Dr. P. Armitage, who suggested the use of Yates's method of assessing the significance of a trend, and to Mrs. Joan Bodington, Miss Muriel Greening, and Miss Keena Jones for the onerous work of filing, coding, and enumerating the questionnaires.

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ORAL CORTISONE THERAPY IN PERIARTHRITIS OF THE SHOULDER

A CONTROLLED TRIAL*

BY

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Periarthritis or capsulitis of the shoulder is a fairly well defined clinical entity characterized by pain in the shoulder region, often extending down the arm, with limitation of all movements at the shoulder-joint, producing in severe cases the "frozen shoulder." One or both shoulders may be affected. There are neither clinical nor radiological signs of arthritis and there is no constitutional disturbance.

The onset of the shoulder lesion is usually spontaneous, but it may sometimes follow trivial trauma, coronary thrombosis, or cerebral vascular lesions. The condition tends to be self-limiting, recovery taking place in six months to three years, but during this period pain may be severe and disability considerable.

Simmonds (1949) found minimal inflammatory changes in the fibrous capsule of the shoulder-joint in cases of this type, and Coventry (1953) believes that the syndrome results from the interaction of pain, disuse, and what he calls the periarthritic personality, but little is really known about the pathogenesis of this condition. It is, however, generally agreed that active movement of the stiff shoulder may expedite recovery, but that it is difficult to persuade the patient to exercise the shoulder adequately, so that adjuvants such as various forms of physiotherapy or x-ray therapy are widely employed. If the shoulder movements are not rapidly regained the stiff shoulder is often manipulated under general anaesthesia.

Sigler and Ensign (1951) and Solomon *et al.* (1951) claimed that short courses of cortisone or A.C.T.H. expedited recovery and reduced the need for manipulation in cases of periarthritis of the shoulder. More recently, Coventry (1953) claimed that a few weeks' treatment with oral cortisone gave most satisfactory

*Based upon a report to the Medical Research Council and Nuffield Foundation Joint Committee on Clinical Trials of Cortisone, A.C.T.H., and Other Therapeutic Measures in Chronic Rheumatic Diseases.

results and reduced the frequency of manipulation under anaesthesia. In view of these claims it seems desirable to report the results of a blind trial in which cortisone was compared with an inert substance in a series of 32 cases.

Selection of Patients

For inclusion in the trial a patient had to have peri-arthritis of one or both shoulders, be over 20 and under 70 years of age, and have no symptoms or signs of disease in other joints. Radiographs of the shoulder had to show no evidence of arthritis or bone disease, the blood sedimentation rate (Wintrobe) had to be under 20 mm. in the first hour, and the chest radiograph had to be within normal limits. Any patient with a history suggesting coronary disease was excluded.

The patients were allocated to two treatment groups, A or B, on a prearranged random order devised separately for those with symptoms of over and under six months' duration, to ensure that cases of short duration would be evenly distributed between the two groups. The treatment register was held by the hospital pharmacist, and the two surgeons admitting patients to the trial and assessing their progress did not know which patients were receiving cortisone until after the whole trial had been completed.

Method of Treatment

Patients allocated to Group B received cortisone acetate suspension made up in syrup to a concentration of 12.5 mg. per ml. The drug was taken orally in four divided doses during the day, and the daily dose was 200 mg. for the first three days, and 100 mg. thereafter until the fourteenth day. The daily dose was then tailed off in decrements of 12.5 mg. every two days, the complete dosage for one four-weeks course being 2.5 g.

Patients allocated to Group A received an inert suspension in similar dosage. This was made from magnesium hydroxide, syrup, and concentrated infusion of quassia. In both appearance and taste it was indistinguishable from the cortisone suspension.

All patients were observed for one week, during which the preliminary investigations were completed; they were then started on the treatment and instructed to exercise their shoulders vigorously, but they were not referred to the department of physiotherapy. At the end of four weeks the patients who had not progressed satisfactorily had their shoulders manipulated under general anaesthesia, the object of the manipulation being to obtain a full range of motion. This manipulation was followed by a second four-weeks course of cortisone or inert suspension, and all cases were followed, where possible, for 18 weeks.

Assessment

The assessment of progress was exclusively clinical and was concerned with pain, range of shoulder movement, and employment status. Both spontaneous pain and pain on movement were recorded in four grades: none (0), slight (1), moderate (2), and severe (3). Range of motion was recorded separately for total abduction, scapulo-humeral abduction, and rotation at the shoulder-joint.

The first assessment was made when the patient was first seen, the second immediately before treatment was started (week 0), and subsequently at the end of the first and fourth weeks of treatment and at the end of the fifth and eighth weeks, and finally at 18 weeks.

Comparability of Treatment Groups

The treatment and control groups were reasonably similar on entry into the trial; thus the 16 patients in the control group comprised 11 males and 5 females whose ages ranged from 45 to 60, with a mean of 52 years; whereas the 16 patients in the cortisone group comprised 7 males and 9 females whose ages ranged from 45 to 70, with a mean of 58 years. The disease duration was not very different.

Thus 15 patients in both groups had a duration of symptoms of one year or less, the mean duration in these 15 patients being 5.1 months in the cortisone group and 6.1 months in the control group. One patient in the cortisone group with a disease duration of nine years made a good recovery, and one patient in the control group with a disease duration of two years made a partial recovery. The mean ratings for pain in the two groups and the mean ranges of shoulder movement both before treatment and on subsequent assessment are shown in Tables I and II, and it will be seen that before treatment the two groups were very simi-

TABLE I.—Mean Grading for Pain

Week:	0	1	4	18
Control group	1.4	1.3	0.8	0.5
Cortisone "	1.4	0.9	0.5	0.6

TABLE II.—Mean Range of Motion in Degrees

Week:	0	1	4	18
Control group:				
Total abduction	75	+14	+17	+48
Shoulder-joint abduction	36	+7	+3	+33
" " rotation	40	+7	+10	+53
Cortisone group:				
Total abduction	82	+21	+22	+28
Shoulder-joint abduction	42	+12	+9	+13
" " rotation	54	+17	+19	+28

lar with regard to pain, but that the cortisone group had by chance a slightly greater range of shoulder movement. Only two patients were completely unable to follow their normal occupation, so that employment status had to be abandoned as a method of assessing progress.

Two patients, both in the cortisone group, were lost to the trial. The first was a man of 69 years with a two and a half months' history of peri-arthritis who died suddenly from coronary occlusion during the third week of treatment. The second was a woman of 53 years who developed follicular dermatitis during the fourth week of treatment and became a defaulter. As a result of these losses the figures for the cortisone group are based on only 15 cases at the end of the fourth week and 14 cases at the eighteenth week.

Results

At the end of the fourth week 11 of the 16 patients in the control group were not progressing satisfactorily and therefore their shoulders were manipulated. Only 6 out of 15 patients in the cortisone group were thought to require manipulation. In one of these patients manipulation was not carried out as she was found to have mitral stenosis. Thus the total number of patients who had their shoulders manipulated and were given a second course of treatment was 16, of which 11 were from the control group.

The behaviour of the two treatment groups in respect of pain was somewhat different. Both started with an identical rating of 1.4, and both ended with a similar rating at eighteen weeks—0.5 as against 0.6. At week 1, the control group showed little change, the reduction in pain being spread throughout the whole period of observation, while in the cortisone group the main reduction in pain occurred between week 0 and week 1, and although there was a further improvement between week 1 and week 4, there was actually a slight deterioration between week 4 and week 18—that is, after treatment had been stopped. Thus, cortisone appears to produce a reduction of pain during the first week of treatment.

In considering the changes in the range of shoulder movement it must be remembered that the cortisone group started with some advantage. Again the end-result at 18 weeks is extraordinarily similar in the control and cortisone groups, but, as with pain, the two groups behave differently during the earlier periods of observation. Thus, in the cortisone group the ranges of movement showed a greater

increase during the first four weeks than between the 4th and 18th weeks, while in the control group the main increase of range occurred during the later weeks.

Thus, a four-weeks course of oral cortisone would seem to have expedited the relief of pain and the recovery of mobility in the shoulder and decreased the number of patients requiring manipulation.

The behaviour of individual patients differed greatly. Although several patients in the cortisone group appeared to improve remarkably during the first week of treatment, at least one patient was completely unrelieved by cortisone; and in the control group at least one patient improved remarkably, although there were several others who remained unrelieved. Because of this great individual variability none of the separate differences between the cortisone and the control groups reach conventional levels of statistical significance. The apparent differences between the two treatment groups might have been related to their differing sex composition, but it has never been suggested that periartthritis behaves differently in the two sexes, and an analysis of the male and female patients separately showed that their shoulders behaved in a like manner.

Tables III and IV show the effect of manipulation and subsequent re-treatment with cortisone and control suspensions. The control group of 11 patients showed a

TABLE III.—Mean Grading for Pain Following Manipulation

Relation to Manipulation:	Before	After	
		1 Week	4 Weeks
Control group (11 cases) ..	0.8	1.6	1.0
Cortisone group (5 cases) ..	0.9	1.1	0.7

TABLE IV.—Mean Range of Motion in Degrees Following Manipulation

Relation to Manipulation:	Before	After	
		1 Week	4 Weeks
Control group (11 cases):			
Total abduction ..	95	+5	+23 123
Shoulder-joint abduction ..	36	+14	+2 52
" " rotation ..	38	+7	+16 61
Cortisone group (5 cases):			
Total abduction ..	92	+9	+13 114
Shoulder-joint abduction ..	53	+5	+13 71
" " rotation ..	78	+2	+28 108

marked increase of pain in the first week after manipulation, which in many cases had not subsided completely by the fourth week following manipulation; whereas the cortisone group of five patients showed only slight or negligible increase of pain in the first week after manipulation. In spite of these marked differences in pain, the range of movement following manipulation continued to increase slowly and equally in both groups.

Discussion

The findings of this trial would seem to confirm previous clinical impressions that a four-weeks course of cortisone may expedite the relief of pain and the recovery of shoulder-joint mobility in cases of periartthritis of the shoulder, and that its use may reduce the number of patients subsequently requiring manipulation under anaesthesia. Furthermore, in patients who have their shoulders manipulated, cortisone therapy appears to reduce the amount of pain experienced during the first few weeks after manipulation. However, some patients appeared to derive no benefit from cortisone therapy in the dosage used in this trial, and, since none of the separate differences between the control and cortisone groups reached conventional levels of statistical significance, the value of cortisone therapy in periartthritis of the shoulder still remains to be proved. In considering the possible advantages of cortisone therapy in this condition it must be remembered that in the present trial cortisone was compared with an inert medicine, whereas in other recent trials (Medical Research Council

and Nuffield Foundation, 1954) cortisone has been compared with simple analgesics such as aspirin or tab. codein. co.

The one death from coronary occlusion is probably not attributable to cortisone therapy, since there is a known association between periartthritis of the shoulder and coronary disease; and in a recent three-year study of 78 patients with periartthritis of the shoulder who did not receive cortisone, Meulengracht and Schwartz (1952) report seven deaths, though not all of these were due to coronary disease.

Summary

In a series of 32 cases of periartthritis of the shoulder the effects of a four-weeks course of oral cortisone have been compared with those of an inert control medicine.

Cortisone therapy appeared to expedite the relief of pain and the recovery of shoulder motion and to reduce the number of patients requiring manipulation, but there was great individual variation in response to treatment, so that none of the differences between the two treatment groups reached conventional levels of statistical significance.

We wish to thank Mr. John Charnley for help in initiating this trial and for referring many of the patients.

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CARCINOMA OF THE CARDIA

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The diagnosis of carcinoma of the cardiac end of the stomach is notoriously difficult in the early stages and, now that surgical resection via a transthoracic approach is a feasible proposition, it is one which it is more than ever important to make. The chief reason for this difficulty is that patients seldom present themselves until they complain of dysphagia, a state of affairs which signifies that there has been involvement of the entry of the oesophagus into the stomach, or that there is spasm of the sphincter secondary to the lesion. True, the lesion may arise at or very near the cardiac orifice and thus cause the patient symptoms at an early stage, but the diagnosis even then can be extremely difficult to establish by such means as oesophagoscopy and barium x-ray films.

Review of the Literature

Most papers concerning carcinoma of the cardia deal with the radiological aspects and the difficulties in arriving at a diagnosis. Garlock (1941) reiterates these and stresses the frequency of dysphagia, often painful, as the presenting symptom, occurring at whatever stage the cardiac orifice is involved. In addition there may be vague indigestion and loss of weight. He mentions persistent back pain, situated to the left of the spine at about the level of the eleventh or twelfth thoracic vertebra as a late symptom. This was not a feature of the cases in the present series. He presents 15 of his own cases, 13 of which had dysphagia.